

**KING & SPALDING**

**King & Spalding LLP**  
**1180 Peachtree Street, NE**  
**Atlanta, Georgia 30309-3521**  
**Tel: (404) 572-4600**  
**Fax: (404) 572-5100**

www.kslaw.com

**F A C S I M I L E**

***Important Notice:** This facsimile transmission is intended to be delivered only to the named addressee, and may contain material that is confidential, proprietary or subject to legal protection or privilege. If it is received by anyone other than the named addressee, the recipient should immediately notify the sender at the address and telephone number set forth herein and obtain instructions as to the disposal of the transmitted material. In no event should such material be read or retained by anyone other than the named addressee, except by express authority of the sender or the named addressee.*

**DATE: May 13, 2008 (4:52 PM)**

<b>Recipient</b>	<b>Company</b>	<b>City/State</b>	<b>Telephone #</b>	<b>Fax #</b>
Examiner Ton	USPTO		571-272-0736	571-273-0736

**FROM:** Susanne Hollinger

7840

**Our Ref. #:** 10758.105015

**NUMBER OF PAGES (Including Cover Page):**

---

**MESSAGE:**

Examiner Ton:

Attached are proposed claim amendments for discussion tomorrow. We hope that these address some of the issues raised in the office action.

Best,  
Susanne

---

Please check that all pages are received. In case of problems, please call **SUSANNE HOLLINGER** at **404-572-2485**.

All return telecopy messages should be sent to **(404) 572-5100**. Thank you.

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Application No.: 10/080,713 Confirmation No.: 9155  
Appellants : Alan Colman et al.  
Filed : February 25, 2002  
  
TC/A.U. : 1600/1632  
Examiner : Thaian N. Ton  
  
Title : Method of Preparing a Somatic Cell for Nuclear Transfer  
  
Docket No. : 10758.105015  
Customer No. : 20786

Commissioner for Patents  
P. O. Box 1450  
Alexandria, VA 22313-1450

June 13, 2008

**AMENDMENT AND RESPONSE TO NON-FINAL OFFICE ACTION**

Sir:

In response to the Non-final Office Action mailed December 13, 2007, please enter the following amendments and consider the enclosed remarks. A petition for extension of time up to, and including June 13, 2008 is enclosed.

**Amendments to the claims** are reflected in the listing of claims beginning on page 2 of this paper.

**Remarks and Arguments** begin on page            of this paper.

## **Amendments to the Claims**

Claims 1-61 (Canceled)

Claim 62. (Currently Amended) A method for producing a non-human transgenic mammal, the method comprising:

- (a) modifying the nuclear genome of a fibroblast or other somatic cell that has a sufficient lifespan to be useful for genetic modification, with wherein the genome has a normal karyotype, at an endogenous locus by a genetic targeting event;
- (b) transferring the modified nuclear genome of the somatic cell to an enucleated oocyte, two cell embryo or zygote which is capable of producing a viable nuclear transfer unit;
- (c) activating the nuclear transfer unit thereby producing an embryo;
- (d) transferring the embryo to a final surrogate mother which is a suitable host for the animal to be grown to term; and
- (e) allowing the embryo to develop to term, thereby producing a non-human transgenic mammal.

Claim 63 (Previously Presented) The method of claim 62, wherein the transgenic mammal is a transgenic sheep, cattle, goat, pig, horse, camel, rabbit or rodent.

Claim 64 (Canceled)

Claim 65 (Previously Presented) The method of claim 62, wherein the genetic targeting event results in removal of a gene, modification of a gene, upregulation of a gene, gene replacement or transgene placement.

Claim 66 (Previously Presented) The method of claim 62, wherein the genetic targeting event results in inactivation of a gene.

Claim 67-69 (Canceled)

Claim 70 (Currently Amended) The method of claim 62, wherein the modification comprises placing a transgene promoter adjacent to an endogenous promotergene in the nuclear genome.

Claim 71 (Previously Presented) The method of claim 70, wherein the promoter is a collagen gene promoter.

Claim 72 (Previously Presented) The method of claim 70, wherein the promoter is a milk protein gene promoter.

- Claim 73 (Previously Presented) The method of claim 70, wherein the promoter directs expression of at least one gene in fibroblast cells.
- Claim 74 (Canceled)
- Claim 75 (Previously Presented) The method of claim 62, wherein the modification comprises placing a marker gene at the endogenous locus in the nuclear genome.
- Claim 76 (Previously Presented) The method of claim 75, wherein the marker gene is a gene that confers resistance to a drug.
- Claim 77 (Previously Presented) The method of claim 76, wherein the gene that confers resistance to a drug is selected from the group consisting of neomycin, G418, hygromycin, zeocin, blasticidin and histidinol.
- Claim 78 (Previously Presented) The method of claim 75, wherein the marker gene is selected from the group consisting of HPRT, gpt, a visible marker gene and a gene that can be detected with a single chain antibody/hapten system.
- Claim 79 (Previously Presented) The method of claim 78, wherein the visible marker gene is GFP.
- Claim 80-81 (Canceled)
- Claim 82 (Previously Presented) The method of claim 62, wherein the genetic targeting event is mediated by lipofection.
- Claim 83-86 (Canceled)
- Claim 87 (Previously Presented) The method of claim 62, wherein the somatic cell is an epithelial cell, a fibroblast cell, an endothelial cell or a muscle cell.
- Claim 88 (Previously Presented) The method of claim 62, wherein the somatic cell is a G<sub>0</sub> cell.
- Claim 89 (Previously Presented) The method of claim 88, wherein the G<sub>0</sub> cell is obtained by serum starvation of a somatic cell.
- Claim 90 (Currently Amended) A method for producing transgenic offspring from a transgenic mammal, the method comprising:
- (a) modifying the nuclear genome of a fibroblast other somatic cell that has a sufficient lifespan to be useful for genetic modification, with wherein the genome has a normal karyotype, at an endogenous locus by a genetic targeting event;
- (b) transferring the modified nuclear genome of the somatic cell to an enucleated oocyte, two cell embryo or zygote which is capable of producing a viable nuclear transfer unit;

- (c) activating the nuclear transfer unit thereby producing an embryo;
- (d) transferring the embryo to a final surrogate mother which is a suitable host for the animal to be grown to term;
- (e) allowing the embryo to develop to term, thereby producing a non-human transgenic mammal; and
- (f) breeding the transgenic mammal to produce transgenic offspring from the transgenic mammal.
- Claim 91-98 (Canceled)
- Claim 99 (Previously Presented) The method of claim 90, wherein the genetic targeting event results in removal of a gene, modification of a gene, upregulation of a gene, gene replacement or transgene placement.
- Claim 100 (Previously Presented) The method of claim 90, wherein the genetic targeting event results in inactivation of a gene.
- Claim 101 (Canceled)
- Claim 102 (Currently Amended) The method of claim 90, wherein the modification comprises placing a ~~transgene promoter~~ adjacent to an endogenous gene promoter in the nuclear genome.
- Claim 103 (Previously Presented) The method of claim 102, wherein the promoter is a collagen gene promoter.
- Claim 104 (Previously Presented) The method of claim 102, wherein the promoter is a milk protein gene promoter.
- Claim 105 (Previously Presented) The method of claim 102, wherein the promoter directs expression of at least one gene in fibroblast cells.
- Claim 106 (Previously Presented) The method of claim 90, wherein the modification comprises placing a marker gene at the endogenous locus in the nuclear genome.
- Claim 107 (Previously Presented) The method of claim 106, wherein the marker gene is a gene that confers resistance to a drug.
- Claim 108 (Previously Presented) The method of claim 107, wherein the gene that confers resistance to a drug is selected from the group consisting of neomycin, G418, hygromycin, zeocin, blasticidin and histidinol.
- Claim 109 (Previously Presented) The method of claim 106, wherein the marker gene is selected from the group consisting of HPR-T, gpt, a visible marker gene and a gene that can be detected with a single chain antibody/hapten system.

Claims 132 (Canceled)

- (b) accomplishing successful nuclear transfer to produce the non-human transgenic mammal.
- (a) modifying the nuclear genome of a fibroblast other somatic cell that has a sufficient lifespan to be useful for genetic modification, with wherein the genome has a normal karyotype, at an endogenous locus by a genetic targeting event;

Claim 131 (Currently Amended) A method for producing a non-human transgenic mammal, the method comprising:

Claims 126-130 (Canceled)

Claim 125 (Previously Presented) The method of claim 62 or 90, wherein the endogenous locus is an immunoglobulin gene.

Claim 124 (Previously Presented) The method of claim 99, wherein the gene that is inactivated is  $\alpha$ -1,3 galactosyltransferase.

Claim 123 (Previously Presented) The method of claim 66, wherein the gene that is inactivated is  $\alpha$ -1,3 galactosyltransferase.

Claim 122 (Previously Presented) The method of claim 62 or 90, wherein the genetic targeting event is mediated by transfection.

Claim 121 (Previously Presented) The method of claim 62 or 90, wherein the genetic targeting event is mediated by electroporation.

Claim 120 (Previously Presented) The method of claim 119, wherein the G<sub>0</sub> cell is obtained by serum starvation of a somatic cell.

Claim 119 (Previously Presented) The method of claim 90, wherein the somatic cell is a G<sub>0</sub> cell.

Claim 118 (Previously Presented) The method of claim 90, wherein the somatic cell is an epithelial cell, a fibroblast cell, an endothelial cell or a muscle cell.

Claims 114-117 (Canceled)

Claim 113 (Previously Presented) The method of claim 90, wherein the genetic targeting event is mediated by lipofection.

Claim 111-112 (Canceled)

Claim 110 (Previously Presented) The method of claim 109, wherein the visible marker gene is GFP.

- Claim 133 (Currently Amended) A method for producing transgenic offspring from a transgenic mammal, the method comprising:
- (a) modifying the nuclear genome of a transgenic fibroblast or other somatic cell that has a sufficient lifespan to be useful for genetic modification, with wherein the genome has a normal karyotype, at an endogenous locus by a genetic targeting event;
  - (b) transferring the modified nuclear genome of the somatic cell to an enucleated oocyte, two cell embryo or zygote which is capable of producing a viable nuclear transfer unit;
  - (c) activating the nuclear transfer unit thereby producing an embryo;
  - (d) transferring the embryo to a final surrogate mother which is a suitable host for the animal to be grown to term;
  - (e) allowing the embryo to mature.